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☐	L12	L11 and CD40	6
☐	L11	L10 and hinge	8
☐	L10	L9 and scfv	9
☐	L9	multispecific ligand	15
☐	L8	L7 and C domain	0
☐	L7	L6 and hinge	3
☐	L6	L5 and MIP	3
☐	L5	L4 and chemokine	4
☐	L4	L3 and CD40	7
☐	L3	L2 and ligand binding domain	12
☐	L2	tetrabody and scFv	149
☐	L1	vaccibody	3

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 NEWS  5  AUG 30   CA(SM)/CAplus(SM) Austrian patent law changes
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                   truncation
 NEWS  8  SEP 25   CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS  9  SEP 25   CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 10  SEP 25   CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 11  SEP 28   CEABA-VTB classification code fields reloaded with new
                   classification scheme
 NEWS 12  OCT 19   LOGOFF HOLD duration extended to 120 minutes
 NEWS 13  OCT 19   E-mail format enhanced
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 NEWS 15  OCT 23   CAS Registry Number crossover limit increased to 300,000 in
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 NEWS 16  OCT 23   The Derwent World Patents Index suite of databases on STN
                   has been enhanced and reloaded
 NEWS 17  OCT 30   CHEMLIST enhanced with new search and display field

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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=> file caplus, bioeng, biotechno, biotechds, esbiobase
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FILE 'BIOTECHDS' ENTERED AT 17:39:40 ON 02 NOV 2006

FILE 'ESBIOBASE' ENTERED AT 17:39:40 ON 02 NOV 2006

=> s (tetrabody or tetramer) and scFv
L1 86 (TETRABODY OR TETRAMER) AND SCFV

=> s hinge and ligand
L2 1444 HINGE AND LIGAND

=> s l1 and l2
L3 1 L1 AND L2

=> d l3 bib abs 1

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:581569 CAPLUS
DN 125:245193
TI Multivalent antibody fragments with high functional affinity for a tumor-associated carbohydrate antigen
AU Rheinnecker, Michael; Hardt, Christina; Ilag, Leodevico L.; Kufer, Peter; Gruber, Rudolf; Hoess, Adolf; Lupas, Andrei; Rottenberger, Christine; Plueckthun, Andreas; Pack, Peter
CS MorphoSys GmbH, Munich, Germany
SO Journal of Immunology (1996), 157(7), 2989-2997
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB The authors report a human-derived self-assembling polypeptide based on the tetramerization domain of the human transcription factor p53, which can be fused to single-chain Fv Ab (scFv) fragments via a long and flexible hinge sequence of human origin, allowing exploitation of the functional affinity increase of binding to a ligand or cell surface with multimeric binding sites. This polypeptide was applied to the construction of a tetrameric scFv against the tumor-associated carbohydrate Ag Lewis Y (Fucα1→2Galβ1→4[Fucα1→3] GlcNAcβ1→3R). For comparison purposes, the corresponding scFv and dimeric mini-antibody, comprising the scFv fused via a flexible murine hinge to an artificial dimerization domain, were also created. The recombinant mini-antibody proteins were expressed in functional form in Escherichia coli and showed the expected m.w. of a dimer and tetramer, resp. Anal. of Lewis Y-binding behavior by surface plasmon resonance revealed specific but very weak binding of the scFv fragment. In contrast, both dimeric and tetrameric scFv fusion proteins exhibited an enormous gain in functional affinity that was greatest in the case of the tetrameric mini-antibody.

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=> s L1 and hinge
L4            5 L1 AND HINGE

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS'
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L5             4 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)

=> d l5 bib abs 1-4

L5    ANSWER 1 OF 4  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN    2005-16809  BIOTECHDS
TI    New antibody that binds to the human IL-4 receptor, useful for asthma,
      septic arthritis, dermatitis herpetiformis, chronic idiopathic urticaria,
      ulcerative colitis, scleroderma, hypertrophic scarring;
         antibody production against protein receptor via cell culture for use
         in disease therapy
AU    CARTER P J; ZHOU H
PA    IMMUNEX CORP
PI    WO 2005047331 26 May 2005
AI    WO 2004-US37242 4 Nov 2004
PRAI  US 2003-518166 7 Nov 2003; US 2003-518166 7 Nov 2003
DT    Patent
LA    English
OS    WPI: 2005-367002 [37]
AN    2005-16809  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - An isolated antibody comprising a light chain variable domain
      or a heavy chain variable domain, where the antibody binds to the human
      interleukin (IL)-4 receptor, is new.
           DETAILED DESCRIPTION - An isolated antibody comprising: (a) a light
      chain variable domain comprising a sequence that is at least 80 %
      identical to a sequence of any of the 6 sequences of 109 amino acids (SEQ
      ID Nos. 4, 6, 8, 10, 12 and 14), given in the specification; a sequence
      of at least 15 contiguous amino acids of the sequence cited above; a
      sequence that is encoded by a nucleotide sequence that is at least 80 %
      identical to any of the 6 nucleotide sequences of 327 bp (SEQ ID Nos. 3,
      5, 7, 9, 11 or 13), given in the specification; or a sequence that is
      encoded by a nucleotide sequence that hybridizes under moderately
      stringent conditions to the complement of the nucleotide sequence; or (b)
      a heavy chain variable domain comprising an amino acid sequence selected
      from any of the 24 sequences given in the specification; a sequence of at
      least 15 contiguous amino acids of the sequence cited above; or a
      sequence that is encoded by a nucleotide sequence that hybridizes under
      moderately stringent conditions to the complement of any of the 24
      nucleotide sequences given in the specification. INDEPENDENT CLAIMS are
      included for the following: (1) an isolated polypeptide comprising an
      IL-4 receptor binding portion of the antibody; (2) an isolated nucleic
      acid comprising any one of the nucleotide sequences cited above, or its
      complement, encoding the light or heavy chain of the antibody, or
      encoding a polypeptide comprising an IL-4 receptor binding portion of the
      antibody; (3) a vector comprising the nucleic acid; (4) an isolated cell
      comprising the nucleic acid; (5) making the antibody comprising
      incubating a cell comprising a nucleic acid encoding the light chain of
      the antibody and a nucleic acid encoding the heavy chain of the antibody
      under conditions that allow the cell to express the light chain and the
      heavy chain and that allow the light chain and the heavy chain to
      assemble into the antibody; and isolating the antibody from said cell;
      (6) inhibiting an IL-4 receptor comprising contacting a cell expressing
      an IL-4 receptor with the antibody under conditions that allow the
      antibody to bind to the IL-4 receptor, where the binding of the antibody
      to the IL-4 receptor inhibits signal transduction through the IL-4
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receptor; and (7) treating a condition in a subject comprising administering to the subject an amount of the antibody or the polypeptide effective for treating the condition.

BIOTECHNOLOGY - Preferred Antibody: The isolated antibody comprises a light chain variable domain comprising an amino acid sequence that differs from SEQ ID Number 4 by at least one amino acid substitution selected from S28T, S30N, S30G, S31N, S32D, S32N, A52T, S54Y, T57P, T57S, G93D, S94H, S94R, P96A, P97G, and T99M; a heavy chain variable domain comprising an amino acid sequence that differs from SEQ ID NO:16 by at least one amino acid substitution selected from N58S, Y101W, F102Y, D103T, D103N, D103P, Y104H, Y104N, Y104W, and Y104R, and T99M; or light chain variable domain and the heavy chain variable domain. The antibody is selected from L1H1, L1H2, L1H3, L1H4, L1H5, L1H6, L1HT, L1H8, L1H9, L1H10, L1H11, L2H1, L2H2, L2H3, L2H4, L2H5, L2H6, L2H7, L2H8, L2H9, L2H10, L2H11, L2H12, L2H13, L2H14, L3H1, L4H1, L5H1, and L6H1. The antibody is a human, humanized, or chimeric antibody, or a monoclonal antibody. The antibody is selected from an IgD, IgE, IgM, IgG1, IgG2, IgG3, IgG4, and IgG4 having at least one mutation in a hinge region that alleviates a tendency to form intra-H chain disulfide bond antibody. Preferred Polypeptide: The isolated polypeptide comprises a Fab, F(ab')2, scFv, diabody, triabody, or tetrabody.
Preferred Vector: The vector is an expression vector. Preferred Cell: The isolated cell is a hybridoma or transgenic cell. Preferred Method: In making the antibody, the cell is a hybridoma. The cell is a transgenic cell. In inhibiting an IL-4 receptor, the cell is a human cell. The human cell is in a human.

ACTIVITY - Antiinflammatory; Cytostatic; Dermatological; Anti-arthritic; Antirheumatic; Immunotherapy; Respiratory-Gen; Uropathic. No biological data given.

MECHANISM OF ACTION - Immunotherapy.

USE - The antibody, polypeptide and methods are useful for treating a condition, such as an inflammatory or cancerous condition, e.g. asthma, septic arthritis, dermatitis herpetiformis, chronic idiopathic urticaria, ulcerative colitis, scleroderma, hypertrophic scarring, Whipple's Disease, benign prostate hyperplasia, a lung disorder in which IL-4 receptor plays a role, condition in which IL-4 receptor-mediated epithelial barrier disruption plays a role, a disorder of the digestive system in which IL-4 receptor plays a role, an allergic reaction to a medication, Kawasaki disease, sickle cell disease, Churg-Strauss syndrome, Grave's disease, pre-eclampsia, Sjogren's syndrome, autoimmune lymphoproliferative syndrome, autoimmune hemolytic anemia, Barrett's esophagus, autoimmune uveitis, tuberculosis, cystic fibrosis, allergic bronchopulmonary mycosis, chronic obstructive pulmonary disease, bleomycin-induced pneumopathy and fibrosis, radiation-induced pulmonary fibrosis, pulmonary alveolar proteinosis, adult respiratory distress syndrome, sarcoidosis, hyper IgE syndrome, idiopathic hypereosinophil syndrome, an autoimmune blistering disease, pemphigus vulgaris, bullous pemphigoid, myasthenia gravis, chronic fatigue syndrome, or nephrosis (claimed).

ADMINISTRATION - Dosage is 5 microg-2 mg/kg/day. Administration is intraarticular, intravenous, intramuscular, intralesional, intraperitoneal or subcutaneous.

EXAMPLE - No relevant example given. (148 pages)

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2001:405557 CAPLUS
DN 135:240549
TI Streptabody, a high avidity molecule made by tetramerization of in vivo biotinylated, phage display-selected scFv fragments on streptavidin
AU Cloutier, S. M.; Couty, S.; Terskikh, A.; Marguerat, L.; Crivelli, V.; Pugnieres, M.; Mani, J.-C.; Leisinger, H.-J.; Mach, J. P.; Deperthes, D.
CS Institute of Biochemistry, University of Lausanne, Epalinges, CH-1066, Switz.

SO Molecular Immunology (2001), Volume Date 2000, 37(17), 1067-1077
CODEN: MOIMD5; ISSN: 0161-5890
PB Elsevier Science Ltd.
DT Journal
LA English
AB Phage display is a powerful method of isolating of antibody fragments from highly diverse naive human antibody repertoires. However, the affinity of the selected antibodies is usually low and current methods of affinity maturation are complex and time-consuming. In this paper, the authors describe an easy way to increase the functional affinity (avidity) of single chain variable fragments (scFvs) by tetramerization on streptavidin, following their site-specific biotinylation by the enzyme BirA. Expression vectors have been constructed that enable addition of the 15 amino acid biotin acceptor domain (BAD) on selected scFvs. Different domains were cloned at the C-terminus of scFv in the following order: a semi-rigid hinge region (of 16 residues), the BAD, and a histidine tail. Two such recombinant scFvs directed against the carcinoembryonic antigen (CEA) were previously selected from human non-immune and murine immune phage display libraries. The scFvs were first synthesized in Escherichia coli carrying the plasmid encoding the BirA enzyme, and then purified from the cytoplasmic exts. by Ni-NTA affinity chromatog. Purified biotinylated scFvs were tetramerized on the streptavidin mol. to create a streptabody (StAb). The avidity of various forms of anti-CEA StAbs, tested on purified CEA by competitive assays and surface plasmon resonance showed an increase of more than one log, as compared with the scFv monomer counterparts. Furthermore, the percentage of direct binding of 125I-labeled StAb or monomeric scFv on CEA-Sepharose beads and on CEA-expressing cells showed a dramatic increase for the tetramerized scFv (>80%), as compared with the monomeric scFv (<20%). Interestingly, the percentage binding of 125I-labeled anti-CEA StAbs to CEA-expressing colon carcinoma cells was definitely higher (>80%) than that obtained with a reference high affinity murine anti-CEA mAb (30%). Another advantage of using scFvs in a StAb format was demonstrated by Western blot anal., where tetramerized anti-CEA scFv could detect a small quantity of CEA at a concentration 100-fold lower than the monomeric scFv.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:581569 CAPLUS
DN 125:245193
TI Multivalent antibody fragments with high functional affinity for a tumor-associated carbohydrate antigen
AU Rheinnecker, Michael; Hardt, Christina; Ilag, Leodevico L.; Kufer, Peter; Gruber, Rudolf; Hoess, Adolf; Lupas, Andrei; Rottenberger, Christine; Plueckthun, Andreas; Pack, Peter
CS MorphoSys GmbH, Munich, Germany
SO Journal of Immunology (1996), 157(7), 2989-2997
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB The authors report a human-derived self-assembling polypeptide based on the tetramerization domain of the human transcription factor p53, which can be fused to single-chain Fv Ab (scFv) fragments via a long and flexible hinge sequence of human origin, allowing exploitation of the functional affinity increase of binding to a ligand or cell surface with multimeric binding sites. This polypeptide was applied to the construction of a tetrameric scFv against the tumor-associated carbohydrate Ag Lewis Y (Fucα1→2Galβ1.fwdarw.4[Fucα1→3] GlcNAcβ1→3R). For comparison purposes, the corresponding scFv and dimeric mini-antibody,

comprising the scFv fused via a flexible murine hinge to an artificial dimerization domain, were also created. The recombinant mini-antibody proteins were expressed in functional form in Escherichia coli and showed the expected m.w. of a dimer and tetramer, resp. Anal. of Lewis Y-binding behavior by surface plasmon resonance revealed specific but very weak binding of the scFv fragment. In contrast, both dimeric and tetrameric scFv fusion proteins exhibited an enormous gain in functional affinity that was greatest in the case of the tetrameric mini-antibody.

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:376378 CAPLUS
DN 122:158176
TI Tetravalent miniantibodies with high avidity assembling in Escherichia coli
AU Pack, Peter; Muller, Kristian; Zahn, Ralph; Pluckthun, Andreas
CS Biochemisches Institut, Universitaet Zurich, Zurich, CH-8057, Switz.
SO Journal of Molecular Biology (1995), 246(1), 28-34
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic
DT Journal
LA English
AB The authors designed tetravalent miniantibodies assembling in the periplasm of Escherichia coli. They are based on single-chain Fv fragments, connected via a flexible hinge to an amphiphatic helix which tetramerizes the mol. The amphipathic helix is derived from the coiled coil helix of the transcription factor GCN4, in which all hydrophobic a positions of every heptad repeat have been exchanged to leucine and all d positions to isoleucine. Gel filtration shows tetramer assembly of the miniantibody even at low concns. As expected, the functional affinity (avidity) of the tetravalent miniantibody is higher in ELISA and BIAcore measurements than that of the bivalent construct and the gain is dependent on surface epitope d.

=> s multimer and scfv and hinge
L6 7 MULTIMER AND SCFV AND HINGE

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE'
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PROCESSING COMPLETED FOR L6
L7 2 DUPLICATE REMOVE L6 (5 DUPLICATES REMOVED)

=> d l7 bib abs 1-2

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2002:157379 CAPLUS
DN 136:293206
TI Multimerization of a chimeric anti-CD20 single-chain Fv-Fc fusion protein is mediated through variable domain exchange
AU Wu, Anna M.; Tan, Giselle J.; Sherman, Mark A.; Clarke, Patrick; Olafsen, Tove; Forman, Stephen J.; Raubitschek, Andrew A.
CS Dep. of Mol. Biol., Beckman Res. Inst. of the City of Hope, Duarte, CA, 91010, USA
SO Protein Engineering (2001), 14(12), 1025-1033
CODEN: PRENE9; ISSN: 0269-2139
PB Oxford University Press
DT Journal
LA English
AB A series of single-chain anti-CD20 antibodies was produced by fusing single-chain Fv (scFv) with human IgG1 hinge and Fc regions, designated scFv-Fc. The anti-CD20 scFv-Fc retained its specific binding to CD20-pos. cells and was active in

mediating complement-dependent cytolysis. However, the purified scFv-Fc included multimeric as well as monomeric components as revealed in the size-exclusion HPLC anal. Variant scFv-Fc were constructed incorporating four different hinges between the scFv and Fc regions, or three different linkers in the scFv domain. All formed multimers, with the highest level of multimerization observed in the scFv-Fc with the shortest linker (8 aa). The structural anal. of the scFv-Fc constructed with 18 or 8 aa linkers by pepsin or papain cleavage indicated that the proteins contained a form in which scFv units had cross-paired to form a "diabody". Such a domain exchange or cross-pairing appears to be the basis of the observed multimerization.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 1995:937220 CAPLUS
DN 123:336986
TI Properties of a single-chain antibody containing different linker peptides
AU Alfthan, Kaija; Takkinen, Kristiina; Sizmann, dorothea; Soederlund, Hans; Teeri, Tuula T.
CS VTT Biotechnology and Food Research, Espoo, FIN-02044 VTT, Finland
SO Protein Engineering (1995), 8(7), 725-31
CODEN: PRENE9; ISSN: 0269-2139
PB Oxford University Press
DT Journal
LA English
AB Single-chain antibodies were constructed using 6 different linker peptides to join the VH and VL domains of an anti-2-phenyloxazolone (Ox) antibody. Four of the linker peptides originated from the interdomain linker region of the fungal cellulase CBHI and consisted of 28, 11, 6 and 2 amino acid residues. The two other linker peptides used were the (GGGGS)3 linker with 15 amino acid residues and a modified IgG2b hinge peptide with 22 residues. Proteolytic stability and Ox binding properties of the 6 different scFv derivs. produced in Escherichia coli were investigated and compared with those of the corresponding Fv fragment containing no joining peptide between the V domains. The hapten binding properties of different antibody fragments were studied by ELISA and BIAcore. The interdomain linker peptide improved the hapten binding properties of the antibody fragment when compared with Fv fragment, but slightly increased its susceptibility to proteases. Single-chain antibodies with short CBHI linkers of 11, 6 and 2 residues had a tendency to form multimers which led to a higher apparent affinity. The fragments with linkers longer than 11 residues remained monomeric.